Exhibit 1

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07/532,267 06/01/90 LANDOLFI

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N 11823-18

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ART UNIT	PAPER NUMBER
1812	8

DATE MAILED: 03/23/92

Before the examiner in charge of your application
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication filed on 1-17-92 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), ____ days from the date of this letter. Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☒ Notice of References Cited by Examiner, PTO-892.
2. ☒ Notice re Patent Drawing, PTO-948.
3. ☒ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, Form PTO-152
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____.

Part II SUMMARY OF ACTION

1. ☒ Claims 1-24 are pending in the application.
   Of the above, claims 16-22 and 24 are withdrawn from consideration.
2. ☐ Claims _____ have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 1-15 and 23 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☒ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☐ Acknowledgement is made of the claim for priority under U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____.
13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

1. The Examiner gratefully appreciates applicant's compliance with their Duty of Disclosure, the Disclosure Statement, the cited art, and the completed PTO 1449.

2. First of all it is pointed out that through an inadvertent oversight the examiner's restriction appears to have suggested that claims 1-15 and 23 were directed to immunoligands between the Ig constant region and IL-2; however, claim 11-14 are not restricted to IL-2, but instead encompass immunoligands wherein the ligand are broadly growth-factor like moieties, or presumably, broadly lymphokine-like moiety. In view of such, an election of specie would have been proper; however, no further election will be required at this time.

Applicant's election with traverse of Group I, claims 1-15 and 23 in Paper No. 7 of 1-17-92 is acknowledged. The traversal is on the ground(s) that the groups are so closely related that they should remain in the same application, because they related to immunoligands wherein the ligand is linked to the Ig constant region. This is not found persuasive because relatedness is not a sufficient basis to assume that a restriction should not be made therebetween, particulary when the Examiner has set forth sufficient reason for requiring this restriction. Applicant has not sufficiently establish that the restriction is in error. The requirement is still deemed proper and is therefore made FINAL.

4. The title of the invention is not descriptive. A new title

is required that is clearly indicative of the invention to which the claims are directed.

The following modification to the title is suggested since immunoglobulins per se are not being claimed. Instead of "/Immunoglobulin" it is suggested that "/Immunoligand" be substituted-provided that by the designation "Chimeric Ligand/Immunoglobulin" applicant is using the "/" to designate an alternative name for the protein. If the latter is not the case, then an amendment or clarification of the title is request.

5. First of all it is pointed out that there has been several case law decisions that have held that rejection sunder 35 USC 101 for operative utility, and 35 USC 112 first paragraph for sufficient enablement are often appropriately coupled and judicially accepted; and that such rejections can be combined because there is typically one issue (See In re Gardner, 117 USPQ 396; In re Fouche, 169 USPQ 429; and Ex parte Stevens, 16 USPQ 2d. 1379).

35 U.S.C. § 101 reads as follows:

> "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

The following is a quotation of the first paragraph of 35 USC §112:

> The specification shall contain a written description of the

invention, and of the manner and process of making and using it, in such full clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best made contemplated by the inventor of carrying out his invention.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an enabling disclosure; and because the invention as disclosed and claimed in inoperative and non-enabling, and therefore lacks patentable utility.

First of all applicant's invention appears to rely on the use ~~would~~ of novel cell lines that produce chimeric molecules/immunoligands wherein the immunoligands require specific portions of immunoglobulins (Ig) that possess specific regions that possess required functional properties. In view of such unique properties, the reproduction of such, in the absence of a deposit, would require undue experimentation to reproduce such altered Ig (immunoligands) that possess the desired physical

and functional properties. Therefore, it is suggested that applicants comply with all of the provisions of MPEP 608.01 (p)(c) regarding deposit of biological material. Assurance of compliance may be an the form of a Declaration or averment under oath.

Secondly, at page 4 general reference is made to growth-factor like moiety; and page 7 merely list several lymphokines and growth factor that can be used as the ligand. However, only one immunoligand was prepared wherein IL-2 was the ligand while this specific immunoligand has a disclosed utility, the specification ~~is non-enabling~~ is non-enabling for the preparation of immunoligands broadly, nor is it evident that the scope of these immunoligand would have a utility and possess the desired physical and functional properties for each portion of the immunoligand. Lymphokine (LK) is generic, and represent a broad and diverse group of proteins that are functionally and patentably distinct, such that the preparation of an immunoligand with one LK such as IL-2 can not effectively predict or enable the preparation and usefulness of the entire scope of LK. Since the corresponding receptors for these LK have different structural motifs, the interaction of a LK to its corresponding receptor differs as well as the signal transducing properties. Therefore, the presence of an Ig portion conjugated to the LK may present a problem for the ligand (L) to receptor interaction.

Antagonist and lymphokine inhibitors are also different from the L per se. Furthermore, applicant's specification fails to provide sufficient guidance in the absence of a sufficient number of enabling examples that cover the scope of the ligands.

Furthermore, the scope and intent of growth factor-like ligand has not been clearly define. "Like" in what respect and degree. In view of the specifics that were disclosed for the particular IL-2/IgG1, it would appear that specific portion of the IL-2 and IgG1 are necessary for the preparation of functionally active immunoligand that possess the desire activity (See pgs 5, and 18-20 of the specification)

Claims 1-15 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

Claims 1-15 and 23 relative to the deposit issue are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

And claims 1-7, 11-14 and 23 are rejected under USC 101 because the disclosed and claimed invention is inoperative and therefore lacks demonstrated and patentable utility; and the claim are rejected under 35 USC 112, first paragraph, for the reasons set forth in the objection to the specification.

6. Claims 1-15 are rejected under 35 U.S.C. § 112, first and second paragraphs, as the claimed invention is not described in such full, clear, concise and exact terms as to enable any person

skilled in the art to make and use the same, and/or for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-7, and 23 are broad and indefinite with regard the scope and intent of "ligand component", because this term does not make clear that all or a portion of the ligand is contemplated; or if the two words are used to collectively describe one part of the immunoloigand. In a similar manner, claims 1, 5-7 and 23 are broad, indefinite and confusing in the use of "constant region component".

Claims 11-14 and 23 are broad, indefinite and confusing in the use of "growth-factor-like". Like in what respect? These claims are also broad and indefinite in the use of "moiety".

7. Claims 4, and 12-14 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 4 is indefinite in the use of improper Markush language according to MPEP 706.03(Y); therefore, it is suggested that the claim be amended as follow; "...component selected from the group consisting of a hinge region...."

Claim 12 is indefinite and incomplete because there is no antecedent basis in claim 11 for "the ligand component" per se because independent claim 11 specifically refers to a "growth

factor-like moiety.

Claim 13 is indefinite, contradictory and fails to have antecedent basis in the earlier portion of the claim for "the growth-factor-like moiety", because the claim initially referred to a "lymphokine like moiety". These two terms are not exactly the same.

Claim 14 is indefinite and does not have antecedent basis in claim 12 for "the heavy chain constant region..."

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this

section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

Claims 1-2, 6-7 are rejected under 35 U.S.C. § 102(a or b) as anticipated by or, in the alternative, under 35 U.S.C. § 103 as obvious over Traunechker et al or Schnee et al or von Wussow

Applicants claims are directed to immunoligands wherein an Ig constant region is linked to the ligand. Although not referred to as immunoligands, the prior art disclose Ig fused to a protein such as TPA, interferon or Interleukin 1c from von Wussow), and the CD4 antigen that are considered ligands within the meaning of the claims (See the abstract of each).

9. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

The other art listed on the PTO 892 is cited as of interest.

10. The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1812.

11. Any inquiry concerning this communication should be directed to Exm. G. D. Draper at telephone number (703) 308-0196.

Draper/tf
February 26, 1992

GARNETTE D. DRAPER
PRIMARY EXAMINER
ART UNIT ~~186~~ 1812